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(Accepted 22 November 1993)

Lesson of the Week

Unsuspected *Pneumocystis carinii* pneumonia and vertically acquired HIV infection in infants requiring intensive care

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Infants with *Pneumocystis carinii* pneumonia may be the first family members to be diagnosed as having HIV infection, particularly as some mothers are unaware of their own infection

The condition of infants with acute respiratory distress may deteriorate to the point of needing assisted mechanical ventilation, particularly during seasonal outbreaks of respiratory syncytial virus infection. In some of these children the course of their illness may have been complicated by secondary bacterial infection or aspiration of gastric contents. Alternatively, the underlying infection may have been particularly virulent or the host unusually susceptible—for example, infants with some degree of chronic lung disease of prematurity or an underlying congenital heart disease. In practice, having excluded respiratory syncytial virus, most physicians choose antimicrobial treatment to cover the common community acquired respiratory pathogens in the age group. We describe three such cases in infants aged 8 weeks, 4 months, and 5 months in whom the aetiological agent and underlying disease—*Pneumocystis carinii* pneumonia and vertically acquired HIV infection—were unsuspected as their condition deteriorated.

Case reports

CASE 1

An 8 week old black girl was admitted to a general paediatric ward with a brief history of irritability and vomiting after feeding. When aged 4 weeks she had been admitted and treated with antibiotics for seven days. On this occasion she was tachypnoeic with a respiratory rate up to 80 breaths/minute. She was later noted to be hypoxic breathing room air and was treated with supplemental oxygen. Throughout her initial stay in hospital she received intravenous cefuroxime. The working diagnosis was an acute respiratory illness

complicated by aspiration of gastric contents. On general examination her length and weight were just above the 10th centile for age and her head circumference was between the 50th and 90th centile. She had a palpable spleen tip.

One week after admission her breathing deteriorated to the point of needing endotracheal intubation and mechanical ventilation. After initial management and stabilisation in a general intensive care unit she was transferred to this paediatric intensive care unit by the transport team. Results from blood tests showed consistently low lymphocyte counts (around $1.89 \times 10^9/l$) and a series of chest x ray films showed a progressive diffuse interstitial lung process (figure). *P. carinii* pneumonia was confirmed by bronchoalveolar lavage and HIV positivity by serum testing.

CASE 2

A 5 month old white girl was admitted to a general paediatric ward with a brief history of low grade fever, cough, and difficulty in feeding. She had been admitted previously with an apparent infection. On this occasion she was noted to be tachycardiac and tachypnoeic (respiratory rate 50-60 breaths/minute), with an audible expiratory grunt. On general examination her length and weight were just above the 10th centile for age and her head circumference was on the 50th centile. She had a palpable spleen tip and her liver was 2 cm below the costal margin. As in case 1, her condition deteriorated until she required endotracheal intubation and mechanical ventilation. Nasopharyngeal aspirate was tested to exclude respiratory syncytial virus and she was treated with intravenous flucloxacillin and ampicillin. Results of blood tests showed consistently

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BMJ 1994;308:462-3

Case 1: Radiographs showing initial diffuse interstitial lung disease (left), which progressed to bilateral "white outs" with visible air bronchograms

low lymphocyte counts ($1.37 \times 10^9/l$), and a series of chest x ray films showed progressive bilateral shadowing in the middle and upper zones. After transfer *P carinii* pneumonia was confirmed by bronchoalveolar lavage and HIV positivity by serum testing.

CASE 3

A 4 month old black boy was admitted to a general intensive care unit with a bronchiolitis-like illness which necessitated supportive treatment with endotracheal intubation and mechanical ventilation. He was known to the hospital, having been born prematurely at 29 weeks' gestation and discharged when aged 6 weeks. On this occasion, he was transferred within 24 hours of admission to this paediatric intensive care unit, where he was gradually weaned from all supportive treatment over the next three days. Results of blood tests showed normal lymphocyte counts (range $3.45-5.07 \times 10^9/l$) and a series of chest x ray films, though not normal in appearance, showed progressive improvement.

Four days later his respiratory distress worsened and he required further supportive treatment. A chest x ray film then showed extensive shadowing in both lung fields. Bronchoalveolar lavage fluid contained *P carinii* pneumocysts. In contrast to the previous week, lymphocyte counts were consistently low (range $0.44-1.52 \times 10^9/l$). HIV positivity was confirmed by serum testing.

Discussion

Microbiological examination of bronchoalveolar lavage fluid from these infants confirmed our clinical suspicion of *P carinii* pneumonia. Although *P carinii* pneumonia is not synonymous with HIV infection and it may be associated with other underlying congenital T cell disorders, we now ask more direct questions about risk factors for HIV infection during history taking and undertake counselling and HIV screening when it has been diagnosed. Unfortunately the cause of the acute pneumonic illness and underlying disease in all three of these infants was unsuspected for at least the first week of inpatient management. An invasive investigation—non-bronchoscopic bronchoalveolar lavage—was prompted solely by the clinical course, which was characterised by unexplained progressive respiratory deterioration, failure to respond to standard treatment, and chest x ray films showing a predominantly interstitial process.

At initial presentation the infants did not appear severely ill, apart from their respiratory distress. Their growth was not retarded, though there were some indicators of possible immunodeficiency. Two of them had abnormally palpable spleens and low peripheral blood lymphocyte counts. We do not know whether the patient in case 3 had an initial viral illness followed by *P carinii* pneumonia or whether the illness was all due to *P carinii* in a child who was becoming progressively immunodeficient. We would now further investigate such a chest radiograph showing predominantly interstitial lung disease even if the patient had responded to initial treatment and although this may seem like "treating" the radiograph rather than the patient.

All three infants were seen over a month. In case 1 the diagnosis was suspected and specific treatment started as soon as the chest radiographs, results, and examination were reviewed by the transport team. Heightened clinical awareness of the diagnosis meant that we followed the strict guidelines on handling blood and body fluids throughout management. Unfortunately, unsafe practices could still occur if those caring for such infants, which includes staff from several disciplines (accident and emergency,

paediatrics, anaesthetics, intensive care, nursing), are unfamiliar with this pattern and cause of severe respiratory disease in early infancy.

We have learnt several lessons from this experience. Firstly, an unexplained progressive respiratory deterioration with poor response to standard treatment necessitates further investigation.

Secondly, an atypical chest radiograph showing a predominantly interstitial process should be definitively explained.

Thirdly, *P carinii* pneumonia should be considered in the differential diagnosis of acute respiratory disease in infancy. Practically, we now use bronchoalveolar lavage early rather than late in investigation; in infants less than 1 year of age this procedure can be performed non-bronchoscopically by means of a narrow bore catheter inserted down the endotracheal tube.^{1,2} Having established a diagnosis of *P carinii* pneumonia, we specifically investigate for a congenital immunodeficiency and counsel the parents about HIV infection, knowing that if diagnosed in their child there are implications for the whole family. *P carinii* pneumonia is now the most common indicator of AIDS, occurring in 40% of children with vertically acquired HIV infection in the British Isles (V Novelli, unpublished data). Presentation is usually in the first six months of life and the prognosis is poor, with a three month survival of only 38%. The infants are often the first family members to be diagnosed as having HIV infection—in inner London only 20% of pregnant women infected with HIV are known by their obstetricians to be infected.³ In all of our cases the mothers had been unaware of their own HIV infection, and the initial history taking had not highlighted a special risk, which perhaps in part accounts for the clinical delay in considering *P carinii* pneumonia in their infants.

Finally, because acute respiratory distress deteriorating to the point of needing mechanical ventilation may be the presenting illness for various congenital and acquired conditions we recommend that all such infants be managed in units where special investigative facilities, skills, and full supportive treatment are available. Our specific treatment for *P carinii* pneumonia includes intravenous co-trimoxazole (trimethoprim 5 mg/kg/dose, six hourly) for 21 days and methylprednisolone (2 mg/kg/day) for 14 days, with subsequent reduction over seven days. With this regimen two infants survived (cases 1 and 3) but the other died.

SUMMARY

When an infant develops acute respiratory failure of sufficient severity to necessitate supportive mechanical ventilation a cause should always be sought. A chest radiograph showing predominantly interstitial lung disease and an infant's failure to respond to standard antibiotic treatment are indications for non-bronchoscopic bronchoalveolar lavage. If *P carinii* pneumonia is diagnosed a congenital immunodeficiency should be sought and the parents counselled about HIV infection. Earlier investigation may be indicated by features of immunodeficiency when taking a history, performing a general examination, or analysing the results of basic haematological testing.

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(Accepted 23 July 1993)